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CONTRACEPTIVE TECHNOLOGY UPDATE®

A Monthly Update on Contraception and Sexually Transmitted Diseases

AHC Media LLC

IN THIS ISSUE

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Recession impacts women's choices — How is your facility responding?

About 1 in 4 have delayed care in past year to save money

Check the records of women who are scheduled to return to your facility for a contraceptive refill or annual well woman exam. Are you seeing empty spots in the schedule?

New national survey data indicate you will. Nearly one in four women have put off a gynecologic or birth control visit in the past year to save money, and the same proportion report having a harder time paying for birth control than they did in the past, according to 2009 information from the Guttmacher Institute.[1] While nearly half of the women surveyed said they want to delay pregnancy or limit the number of children they have due to the impact of the recession, economic hardship is causing many of them to skimp on their contraceptive use in order to save money.

The recession has put many women, including middle-class women who are having trouble making ends meet, in an "untenable situation,"

Gardasil approved for use in males — Cervarix gets OK for use in females

Both recommended for Vaccines for Children coverage

Two new actions from the Food and Drug Administration (FDA) will impact your practice. The agency has given the nod to use of the Merck & Co. quadrivalent vaccine Gardasil for the prevention of genital warts (condyloma acuminata) due to human papillomavirus (HPV) types 6 and 11 in boys and men ages 9-26. The FDA also has approved the GlaxoSmithKline Cervarix bivalent vaccine for use in the prevention of cervical precancers and cervical cancer associated with oncogenic HPV types 16 and 18 for use in girls and young women ages 10-25.

*(See **Gardasil and Cervarix**, continued on page 136)*

says **Sharon Camp**, PhD, Guttmacher president and CEO. Women want to avoid unintended pregnancy more than ever, but at the same time are having difficulty affording the out-of-pocket costs of prescription contraception, she adds.

"Unfortunately, while delaying a prescription refill or skipping pills may save women money in the short term, it increases their risk of an unintended pregnancy and results in greater costs related to abortion and unplanned birth later on," she states.

Further information is scheduled to be released this month says **Laura Lindberg**, PhD, a senior research associate at Guttmacher. Surveys from about 50 Title X family planning clinics will be analyzed for shifts in client types and numbers, staffing, and funding during the recession, she states.

What do women say?

Conducted in July and August, the Guttmacher survey includes responses from a nationally representative sample of some 1,000 low- and middle-income sexually active women. Designed to determine how the current economy has affected women and their families, researchers gathered women's views of contraceptive use, ability to access contraceptives, and their decisions on whether or when to have a child. Women included in the survey were in the 18-39 age range and had annual household incomes of less than $75,000.

More than one in four women or their partners reported lost jobs or health insurance in the past year, and many say they have lost confidence in their ability to provide for their families, survey findings indicate. Fifty-two percent of surveyed women said they are earning less or financially doing worse than they were a year ago. According to the Guttmacher report, these financial setbacks are occurring evenly across various groups of American women; there are no significant differences in the reported share of women who are financially worse off by age, education, marital status, race or ethnicity, region of the country or

EXECUTIVE SUMMARY

Nearly one in four women have put off a gynecologic or birth control visit in the past year to save money, and the same proportion report having a harder time paying for birth control than they did in the past, according to 2009 information from the Guttmacher Institute.

- While nearly half of the women surveyed said they want to delay pregnancy or limit the number of children they have due to the impact of the recession, economic hardship is causing many of them to skimp on their contraceptive use in order to save money.
- Eight percent of women said they sometimes did not use birth control in order to cut costs.

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Editor: **Rebecca Bowers**.
Associate Publisher: **Coles McKagen** (404) 262-5420 (coles.mckagen@ ahcmedia.com).
Senior Managing Editor: **Joy Daughtery Dickinson** (229) 551-9195 (joy.dickinson@ahcmedia.com).
Director of Marketing: **Schandale Kornegay**.
Senior Production Editor: **Nancy McCreary**.

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Editorial Questions

Questions or comments?
Call **Joy Daughtery Dickinson** (229) 551-9195.

household income.[1]

With less money in hand, women are making risky choices when it comes to contraception. Eight percent of women said they sometimes did not use birth control in order to save money; researchers found this cost-cutting behavior was more common among those who were financially worse off than among others (12% vs. 4%). For those women using oral contraceptives, 18% reported inconsistent use as a means of saving money. Pill users said they skipped pills (4%), delayed getting a prescription filled (12%), went off the Pill for at least a month (11%), and obtained fewer pill packs at one time (8%). Again, women in less fortunate straits were more apt to have inconsistent use (25% vs. 6%).[1]

Clinics feel the pinch

Eleven percent of women surveyed in the Guttmacher Institute report say they have switched to a less expensive provider for their reproductive health care services.

"We are seeing more women in their 30s and 40s that depended on us in their 20s return for care," says **Sarah Stoesz**, president and CEO of Planned Parenthood Minnesota, North Dakota, South Dakota. "For many of these women, our doctors are the only ones they see all year."

Stoesz reports that more patients are telling her nurse practitioners that they have lost their jobs and insurance benefits or have had their hours cut back at work. Of particular note is the increase in women requesting long-term contraception, specifically intrauterine devices — up more than 50% over last year, she notes. Such developments are not unusual; Los Angeles County, Planned Parenthood reports that in the first three months of 2009, requests for intrauterine devices were up 83% over the same period in 2008.[2]

Planned Parenthood of the Great Northwest (PPGNW) in Seattle reports a 35% jump in patient demand from 2008. PPGNW health centers in Washington were seeing more than 9,400 patients a month as of Spring 2009.[3] To be more effective in serving patients, the organization has instituted electronic medical records with their affiliates and a centralized contact center for appointments and follow-ups.[3]

What are clinics doing to help women stay on course when it comes to contraception? About 15% of Planned Parenthood affiliates offer the "Pills Now. Pay Later" program, where women can come into a health center for a quick visit and leave with a year's worth of birth control pills, says **Tait Sye**, Planned Parenthood spokesman. The center will bill a patient's pills to her credit card, check card, or flex spending card on a monthly basis, with fees guaranteed not to increase over the course of the prescription.

What's the next step?

The demand for health care assistance isn't about to fade away. A September 2009 U.S. Department of Health and Human Services analysis of U.S. Census data reveals the number of uninsured Americans increased from 39.8 million in 2001 to 46.3 million in 2008. The numbers do not include those who have lost their insurance during the recent recession or who had coverage gaps shorter than one year.[4]

Nowhere is the need for health care reform more evident than in rural Minnesota, says Stoesz. More than 94% of Planned Parenthood's 64,000 patients are women, and nearly 60% live in rural Minnesota.[5] Poverty, lack of insurance, and limited access to health care combines to result in poorer outcomes for Minnesota's rural women, especially when it comes to reproductive health, states Stoesz. Fewer rural women receive recommended preventive gynecological care, including mammograms and breast, cervical, and colorectal cancer screening than do their urban peers.

How are organizations working with women who might be facing increased financial pressures due to the recession?

"Planned Parenthood utilizes a variety of appropriate funding streams designed to broaden access to family planning services," says Stoesz. "From state and federal programs to philanthropic support, we make sure that women in need of health care are not turned away because of the inability to pay." **(Need ideas for augmenting your facility's funding? See what other clinics are doing in an upcoming issue of *Contraceptive Technology Update*.)**

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Gardasil and Cervarix

(Continued from cover)

Gardasil currently is approved for use in girls and women ages 9-26 for the prevention of cervical, vulvar, and vaginal cancer caused by HPV types 16 and 18; precancerous lesions caused by types 6, 11, 16, and 18; and genital warts caused by types 6 and 11. Cervarix is the second vaccine approved for HPV prevention in women. **(To read more about both vaccines, see the *Contraceptive Technology Update* article, "HPV vaccine update: Will there be more options for women and men?" November 2009, p. 121.)**

Cervarix now joins Gardasil as the second of two vaccines recommended by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) for prevention of cervical cancer in females. The recommendation was issued at the committee's October 2009 meeting.

ACIP did not call for routine use of Gardasil in males. Instead, it voted to approve the statement "the quadrivalent HPV vaccine may be given to males aged 9 through 26 years to reduce their likelihood of acquiring genital warts."[1] This "permissive use" guidance means that Gardasil may be given to males ages 9-26 to reduce the likelihood of acquiring genital warts at the discretion of the patient's health care provider.

Cervarix and Gardasil earned the committee's recommendation for coverage under the Vaccines for Children (VFC) program, which pays for uninsured and underinsured children through age 18. The ACIP recommendations do not result in requirements for vaccine administration by individual states or coverage by insurance companies; however, state health authorities and private insurers typically follow the committee's guidance.

Extend use to males

Nearly 17,000 new cases of genital HPV infection, of any type, occur each day in U.S. males and females, says **Anna Giuliano**, PhD, professor of medicine and epidemiology at the University of South Florida and a program leader in the Risk Assessment, Detection, and Intervention program at Moffitt Cancer Center in Tampa. While most of the infections clear on their own, it is estimated that 1 million people in the United States will develop genital warts, which can cause discomfort and be distressing, observes Giuliano. While some resolve without treatment, warts recur in at least one-quarter of cases that require care.

Gardasil helps protect against the four types of HPV (6, 11, 16, and 18) that cause the most disease. It is estimated that HPV types 16 and 18 account for 70% of cervical and vaginal cancer cases and up to half of vulvar cancer cases; types 6 and 11 cause about 90% of all genital warts cases.

To address any funding challenges that might impede access to vaccination for those not in the VFC-eligible age range, Merck will extend its assistance program to cover uninsured males ages 19-26. The program, established in 2008, provides Gardasil free of charge to women of similar ages who meet the program criteria.

Merck plans to extend its Gardasil patient rebate and dose replacement programs to eligible privately insured males with partial or no coverage. The rebate program enables those qualifying people ages 19-26 with private insurance whose out-of-pocket costs are more than $30 to receive a rebate from Merck for up to a maximum of $130 per dose. The dose replacement program provides a limited number of replacement doses of the vaccine to eligible health care providers who learn after giving the vaccine to a qualifying patient that no reimbursement is available from their private insurance.

Public health officials are weighing the cost-effectiveness of administering Gardasil in men. Results of a just-published analysis state that given currently available information, including boys in an HPV vaccination program "generally exceeds conventional thresholds of good value for money, even under favorable conditions of vaccine protection and health benefits."[2] Information from such cost-benefit analyses led the committee to issue "permissive" use guidance rather than recommendation for routine use.[3]

Cervarix is expected to be commercially available in the United States in late 2009, say company officials. It is administered to young women in a three-dose schedule that should be completed within six months of the initial dose. The most common local adverse reactions and general adverse events reported in clinical trial participants were pain, redness, and swelling at the injection site; fatigue; headache; joint and muscle

ache; and gastrointestinal symptoms.

Public health officials are weighing the evidence when it comes to determining the use of the two available HPV vaccine options in women. At the June 2009 ACIP meeting, research presented from a comparative trial of Gardasil and Cervarix indicates the bivalent vaccine does produce higher titers than the quadrivalent vaccine.[4] Both vaccines produce titers that are substantially higher than those after natural infection; the implications of this, in terms of differences in duration of protection, are unclear, note officials.[4]

At its October 2009 meeting, ACIP members recommended routine vaccination of females ages 11 or 12 with three doses of HPV vaccine for prevention of cervical cancer. The quadrivalent vaccine is recommended for prevention of cervical cancer and genital warts.[1]

The FDA approval of a vaccine such as Cervarix is an important development in the prevention of cervical cancer, says **Levi Downs**, MD, MS, FACOG, assistant professor in the Department of Obstetrics, Gynecology, and Women's Health at the University of Minnesota.

"The treatment of cervical precancers and cancer can be devastating for women and their families," says Downs, who served as a clinical trial investigator for Cervarix. "It's important for a vaccine to help reduce the need for the invasive procedures often used to treat cervical precancers and cancers."

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Options for treatment of heavy bleeding in focus

Clinicians now have an approved indication in hand for use of the levonorgestrel intrauterine system Mirena (LNG IUS, Mirena, Bayer HealthCare Pharmaceuticals; Wayne, NJ), to treat heavy menstrual bleeding in women who use intrauterine contraception as their method of pregnancy prevention. The Food and Drug Administration (FDA) gave approval to the indication in October 2009, which made Mirena the first intrauterine device approved for this additional use. ***(Contraceptive Technology Update* reported on use of the LNG-IUS for treatment of heavy bleeding in the article, "New analysis eyes use of LNG IUS for menorrhagia, September 2009, p. 99.)** Mirena was approved as a contraceptive by the FDA in 2000.

Heavy menstrual bleeding can cause impairment in quality of life for women and represents a common reason women consult clinicians; traditionally, surgery has represented the main therapeutic option, says **Andrew Kaunitz**, MD, professor and associate chair in the Obstetrics And Gynecology Department at the University of Florida College of Medicine — Jacksonville.

With the FDA's approval of use of the LNG IUS for treatment of heavy menstrual bleeding, women with this condition have an effective office-based nonsurgical option, says Kaunitz. Kaunitz presented information from the pivotal trial at the recent Reproductive Health 2009 sponsored by the Association of Reproductive Health Professionals, the Planned Parenthood Federation of America National Medical Committee, and the Society of Family Planning.[1]

Bleeding is lessened

The pivotal trial was a randomized, open-label, active-control, parallel-group study of 160

EXECUTIVE SUMMARY

The intrauterine system Mirena has received an approved indication from the Food and Drug Administration to treat heavy menstrual bleeding in women who use intrauterine contraception.

- Women will have an effective office-based nonsurgical option for heavy bleeding.
- Research indicates a new hormonal combination oral contraceptive using estradiol valerate and dienogest significantly reduces menstrual blood loss in women with heavy and/or prolonged menstrual bleeding. The drug is available in Europe as Qlaira. Its manufacturer is seeking U.S. approval.

healthy women of reproductive age who had confirmed heavy menstrual bleeding and did not have any medical conditions known to cause heavy menstrual bleeding, with the exception of small uterine fibroids in some patients. Heavy menstrual bleeding, defined as menstrual blood loss of greater than or equal to 80 ml, was determined using the alkaline hematin method. Scientists followed 79 women who were randomly selected to receive the LNG IUS and compared them to 81 women were randomized to receive oral medroxyprogesterone acetate (MPA) over six menstrual cycles. Researchers defined successful treatment when two outcomes were met:

- a proportion of subjects with end-of-study menstrual blood loss at less than 80 ml;
- a greater than or equal to 50% decrease in menstrual blood loss from baseline to end of study.

The proportion of women who had been successfully treated (defined as menstrual blood loss of less than 80 ml at end of study) was higher in the LNG IUS group (67/79) relative to women in the MPA group (18/81), study findings indicate.[1] Of the women treated with MPA, fewer than 30% experienced a more than 50% reduction in menstrual blood loss, compared with more than 80% of women treated with the LNG-IUS, who experienced at least a 70% decrease.[1] The study excluded women with organic or systemic conditions that may cause heavy uterine bleeding (except fibroids, with total volume not above 5 ml). The most common reported adverse events for the LNG-IUS in the study were uterine bleeding/spotting at irregular intervals, headache, ovarian cysts, vaginitis, pain during menstruation, pelvic pain, and breast tenderness.[1]

Pill combats bleeding

Science is now eyeing a new hormonal combination oral contraceptive for use in treatment of heavy bleeding. Investigators report that an estradiol valerate/dienogest oral contraceptive (OC) significantly reduces menstrual blood loss in women with heavy and/or prolonged menstrual bleeding without organic pathology.[2]

The combination pill has been available in several European countries since May 2009 for use as a contraceptive under the trade name Qlaira. **(For more information, see the *CTU* article "Research eyes new oral contraceptives," March 2009, p. 31, and "Pill with dienogest progestin under review," August 2008, p. 89.)** Its manufacturer, Bayer, submitted a New Drug Application to the FDA in July 2009. It is seeking approval for two indications: oral contraception and the treatment of heavy and/or prolonged menstrual bleeding in women without organic pathology who desire oral contraception.

Qlaira's progestin component, dienogest, has a particularly good effect on the endometrial functions that control bleeding, observes **Ian Fraser**, MD, professor in reproductive medicine, obstetrics, gynecology, and neonatology at the University of Sydney. The dynamic dosing of Qlaira and its estrogen component, estradiol valerate, are thought to support this action, Fraser notes.

Qlaira's dosing regimen incorporates an estradiol step-down and a progestin step-up designed to provide estrogenic dominance in the first part of the cycle to ensure initial endometrial proliferation and sensitivity for midcycle progestin action.[3] The formulation provides progestin dominance during the mid-to-late part of the cycle to ensure endometrial stability, particularly toward the end of the cycle.[4]

RESOURCE

The National Association of Nurse Practitioners in Women's Health has a webinar on its web site, www.NPWH.org, on heavy menstrual bleeding. Go to the web page and click on the link under "Abnormal Uterine Bleeding Webinar." Participants can earn continuing education and get a tool kit to use in talking with women about heavy bleeding.

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Medical abortion: Safety, access probed

If medical abortion using mifepristone (Mifeprex, Danco Group) and misoprostol is offered at your facility, be sure to review a new study that asserts the safety of a particular mifepristone/misoprostol regimen.[1] According to study results, rates of serious infection decreased at Planned Parenthood facilities after protocol was changed from vaginal to buccal administration of misoprostol, combined with routine administration of antibiotics.

Understand that the risk for infection is small for medical abortion; a 2004 literature review reported the frequency of diagnosed and/or treated infection after such regimens as very low (0.92%, N = 46,421).[2]

The current study is a retrospective analysis assessing the rates of serious infection after medical abortion at some 300 Planned Parenthood facilities. From 2001 through March 2006, most of the health centers used a regimen of oral mifepristone, followed 24-48 hours later by vaginal misoprostol. In response to concern about serious infections, Planned Parenthood revised its protocol in early 2006 and changed the route of misoprostol administration from vaginal to buccal and initiated additional infection-reduction measures. In July 2007, Planned Parenthood began requiring routine treatment with antibiotics for all medical abortions. **(Concerns about infections arose following five deaths in 2005 from serious bacterial infection and sepsis after use of the mifepristone/misoprostol regimen. See the *Contraceptive Technology Update* articles, "Mifepristone label gets new safety information," October 2005, p. 115, and "Update: FDA strengthens mifepristone labeling," March 2005, p. 33.)**

To get providers up to speed on the changes, Planned Parenthood held numerous national teleconferences so that clinicians in different time zones had opportunities to join the call, understand why the changes in the regimen were being made, and give them opportunities to ask questions, says **Mary Fjerstad**, NP, MHS, lead author of the article. The organization also circulated documents throughout the Planned Parenthood system that explained the regimen changes, notes Fjerstad, now senior clinical advisor for the Medical Abortion Initiative at Ipas, a Chapel Hill, NC-based international reproductive health advocacy organization. Fjerstad was a co-presenter of the study findings at the recent Reproductive Health 2009 conference.[3]

Rates of serious infection dropped significantly after the joint change to buccal misoprostol from vaginal misoprostol and to testing for sexually transmitted infection or routine provision of antibiotics as part of the medical abortion regimen, study authors state. The rate declined 73%, from 0.93 per 1,000 abortions to 0.25 per 1,000 [absolute reduction, 0.67 per 1,000; 95% confidence interval (CI), 0.44 to 0.94; $P < 0.001$]. The subsequent change to routine provision of antibiotics led to a further significant reduction in the rate of serious infection: a 76% decline, from 0.25 per 1,000 abortions to 0.06 per 1,000 (absolute reduction, 0.19 per 1000; 95% CI, 0.02 to 0.34; $P=0.03$).[1]

Has access expanded?

Reproductive health advocates held high hopes for the advent of medical abortion in the United States as a means of expanding abortion access to women, particularly those in rural areas. While use of mifepristone has become widespread and has contributed to the shift toward earlier abortions, its use has not improved women's geographic access to abortion services, states a new report.[3]

The number of medical abortions and the number of providers offering mifepristone increased dramatically between 2000 and 2007, even as the total number of abortions performed in the United States declined steadily over this period, the study authors note. In 2007, 902 providers performed 158,000 mifepristone abortions, which represented an estimated 21% of eligible abortions performed that year. However, most of

EXECUTIVE SUMMARY

Results of a new study of the mifepristone/misoprostol regimen of medical abortion indicate rates of serious infection decreased after protocol was changed from vaginal to buccal administration of misoprostol, combined with routine administration of antibiotics.

- A 2004 literature review of medical abortion reported the frequency of diagnosed and/or treated infection after such regimens as very low (0.92%, N = 46,421).
- While widespread use of mifepristone has contributed to the shift toward earlier abortions, its use has not improved women's geographic access to abortion services, a new national report states.

these abortions were performed at or near facilities that also provided surgical abortions, the authors state. Only five mifepristone-only providers of 10 or more abortions were located farther than 50 miles from any surgical provider of 400 or more abortions, findings indicate.

Mifepristone now is an integral part of U.S. abortion service provision, accounting for about one-fifth of very early abortions.[4] Many factors have led to its increased use, says **Rachel Jones**, PhD, senior research associate at the Guttmacher Institute, which reviews reproductive health access. Many abortion providers, particularly those who already were performing surgical abortions, wanted to provide women with options in reproductive health, notes Jones. Also, when the Food and Drug Administration approved mifepristone in 2000, many organizations, such as the National Abortion Federation and Planned Parenthood Federation of America, promoted training for interested health care professionals so they could include early medical abortion in their practices, states Jones. Over time, more providers have become more comfortable with early medical abortion and have added it to their practice or expanded its use, she notes.

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Condom wrap-up — New options for women & men

Good news for patients at your clinic: The second-generation FC2 Female Condom is available for purchase in the United States, which gives American women a nonlatex, female-controlled option in disease protection. Men also have new choices when it comes to nonlatex condoms; two options now are available in the United States.

The Food and Drug Administration gave approval in March 2009 for U.S. sale of the second generation of the female condom manufactured by the Female Health Company (FHC). With the introduction of a new proprietary nitrile material and a less labor-intensive manufacturing process, the company can offer the condom, known as the FC2, at a public health sector cost that is about 30% less than the original FC1 polyurethane condom. **(See the *Contraceptive Technology Update* article "Second-generation female condom approved by FDA; What's next for the U.S.?" June 2009, p. 61.)** The FC2 offers another option to the male condom and is a suitable choice for those with latex sensitivity. Some women have found FC2 quieter than the first-generation FC Female Condom.

EXECUTIVE SUMMARY

The second-generation FC2 Female Condom is now available for purchase in the United States, which gives American women a nonlatex, female-controlled option in disease protection.

- With the introduction of a new proprietary nitrile material and a less labor-intensive manufacturing process, the FC2 condom can be offered at a public health sector cost that is about 30% less than the original FC1 polyurethane condom.
- Men also have new choices when it comes to nonlatex condoms: Durex Avanti Bare and LifeStyles Skyn. Both condoms are made of polyisoprene.

The company announced the U.S. product rollout at company at an October 2009 meeting of the Southeastern Urban Initiative for Reproductive Health, a coalition of reproductive health advocates from Southern states that is seeking increased federal funding for HIV prevention. Reception of the second generation condom by conference participants was "exciting," says **Mary Ann Leeper**, PhD, FHC senior strategic adviser.

FC2 may be purchased from the company's two public sector distributors: Total Access Group (www.totalaccessgroup.com) and Global Protection Corp., (www.globalprotection.com/store). In addition, FHC has launched a web site, www.fc2femalecondom.com, which includes tiered pricing information for ordering a minimum quantity of 25,000 units directly from the company. Price per unit will decline based on the volume purchased, state company officials. The maximum price to purchase FC2 from the company's distributors is $0.82/unit regardless of quantity, which represents approximately a 30% decrease from the unit price paid for FC1.

The new condom will be available in certain

retail outlets. FHC is seeking a partner with appropriate experience to promote FC2 directly to consumers in the United States, says Leeper. Retail outlets are being identified, and the company is negotiating retail sale agreements, she adds.

The company is developing a seeding program to provide free allotments of FC2 Female Condoms to reproductive health service organizations as part of an introductory awareness and education program. The program will include training for health care providers on how to integrate female condom education into reproductive health counseling. Organizations may obtain further information on program enrollment by visiting www.fc2.us.com. The site also offers free resources, such as a training manual, "Safer Is Sexy," a counseling tips handout, and a fact sheet on negotiating condom use.

Consider polyisoprene

Men now have two more options when it comes to nonlatex condoms: Durex Avanti Bare and LifeStyles Skyn. Both condoms are made of polyisoprene. LifeStyles introduced its Skyn condom in July 2008, and the Durex Avanti Bare arrived on market shelves in August 2009.

Both condoms are available in all outlets where condoms are routinely sold. Most drugstores retail Avanti Bare 12 counts for $13.99, says **Stephen Mare**, senior brand manager for Durex Consumer Products.

How do polyisoprene condoms compare with polyurethane condoms? According to Mare, polyisoprene is much softer and more elastic than polyurethane. They are easier to don and provide a supple, natural feel for the user. The result is a very pleasant-feeling condom that most users prefer to polyurethane, Mare says. Polyisoprene condoms react similarly to latex condoms in the presence of oil, so providers should instruct users to use only water-based or silicone lubricants with them.

Are such condoms safe for use in people with latex allergies? While 1%-6% of the U.S. population are believed to be allergic to latex, the prevalence of latex sensitivity is believed to be much higher among health care workers who have repeated exposure to latex-containing medical devices, such as surgical and examination gloves.[1] Ask patients whether they experience itching, rash, or wheezing after wearing latex gloves or inflating a balloon. If you suspect a patient has latex sensitivity, consider recommending synthetic condoms, and refer the patient for allergy skin testing. While latex condom use is contraindicated in patients with general latex sensitivity, synthetic and natural membrane condoms can be recommended for prevention of pregnancy. Only synthetic condoms should be recommended for prevention of sexually transmitted infections, including HIV.[1]

"Dermatological testing shows that Durex Avanti Bare condoms have minimal potential for induced delayed hypersensitivity, also called 'Type IV allergy' and 'allergic contact dermatitis,'" states Mare. "Some people who are sensitive to natural rubber latex may also have a sensitivity to these condoms. Consumers who experience any allergic reaction should stop using them and see a doctor."

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Update care of pregnant women in light of H1N1

As the United States gears up to combat the H1N1 flu (also known as swine flu), be sure your practice includes the latest Centers for Disease Control and Prevention (CDC) recommendations for care of pregnant women.

From April 15 to May 18, 2009, 34 confirmed or probable cases of pandemic H1N1 in pregnant women were reported to CDC from 13 states,

EXECUTIVE SUMMARY

Pregnant women are at higher risk for severe complications and death from influenza, including 2009 H1N1 influenza and seasonal influenza, says the Centers for Disease Control and Prevention. Treatment with oseltamivir or zanamivir is recommended for pregnant women with suspected or confirmed influenza and can be taken during any trimester of pregnancy.

- Teach women to be aware of flu symptoms and the need for early treatment.
- All pregnant women should receive immunization for seasonal flu immediately and H1N1 flu as soon as the vaccine is available. The immunizations pregnant women receive are safe and provide flu protection for themselves and their newborns.

according to a CDC analysis of the outbreak.[1] Eleven (32%) women were admitted to hospitals. The estimated rate of admission for pandemic H1N1 influenza virus infection in pregnant women during the first month of the outbreak was higher than it was in the general population [0.32 per 100,000 pregnant women, 95% CI (confidence interval) 0.13-0.52 vs. 0.076 per 100,000 population at risk, 95% CI 0.07-0.09]. Between April 15 and June 16, 2009, six deaths in pregnant women were reported to the CDC. All were in women who had developed pneumonia and subsequent acute respiratory distress syndrome requiring mechanical ventilation. These data have led the CDC to recommend clinicians to promptly treat pregnant women with H1N1 influenza virus infection with anti-influenza drugs. ***(Contraceptive Technology Update* reported on these recommendations in the June 2009 article, "Interim guidance issued on pregnant women and swine flu," p. 61.)**

Pregnant women are at higher risk for severe complications and death from influenza, including 2009 H1N1 influenza and seasonal influenza, says the CDC. Treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) is recommended for pregnant women with suspected or confirmed influenza and can be taken during any trimester of pregnancy. The duration of antiviral treatment is five days. For oseltamivir, the treatment dosage for adults is one 75 mg capsule twice per day for five days; for chemoprophylaxis, the adult dosage is one 75 mg capsule once per day for 10 days. For zanamivir, the treatment dosage for adults is two 5 mg inhalations (10 mg total) twice per day for five days; for chemoprophylaxis, the adult dosage is two 5 mg inhalations (10 mg total) once per day for 10 days.[2]

Zanamivir might be the preferable antiviral for chemoprophylaxis of pregnant women because of its limited systemic absorption, the CDC states. However, respiratory complications that might be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems. For these women, oseltamivir is a reasonable alternative, says the CDC.[2]

Oseltamivir and zanamivir have been classed as "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess their safety for pregnant women. However, the available risk-benefit data indicate pregnant women with suspected or confirmed influenza should receive prompt antiviral therapy, advises the CDC. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use.

Be sure to initiate treatment as early as possible because studies show that treatment initiated early (i.e., within 48 hours of illness onset) is more likely to provide benefit. Do not delay treatment for laboratory confirmation of influenza, the CDC recommends. Laboratory testing can delay treatment, and a negative rapid test for influenza does not rule out influenza. The sensitivity of rapid tests can range from 10% to 70%, the CDC states.[2]

Talk with pregnant women about signs and symptoms of influenza, and the need for early treatment. In a recent series of pregnant women with 2009 H1N1 influenza, manifestations included fever (97%), cough (94%) rhinorrhea (59%), sore throat (50%), headache (47%), shortness of breath (41%), myalgia (35%), vomiting (18%), diarrhea (12%), and conjunctivitis (9%), similar to those in the general population.[1]

Since rapid access to antiviral medications is essential, health care providers who care for pregnant women should develop methods to ensure that treatment can be started quickly after symptom onset, according to the CDC. They should ensure rapid access to telephone consultation and clinical evaluation for pregnant women; also consider empiric treatment of pregnant women based on telephone contact if hospitalization is not indicated, states the CDC.[2]

ACOG issues guidance

The American College of Obstetricians and Gynecologists (ACOG) has joined a national coalition of health care and information providers for pregnant women and children to get out H1N1 information to patients and providers. The coalition has issued a joint statement to pregnant women, which includes five important messages, which should be shared with your pregnant patients:

- Pregnant women are at increased risk for

COMING IN FUTURE MONTHS

- ■ Provide patient education on vasectomy
- ■ Using Facebook, blogs, and cell phones for STD prevention
- ■ Check new options for HIV testing
- ■ Changes on tap for circumcision guidance?
- ■ Review new HIV primary care guidelines

serious disease and even death from pandemic H1N1 influenza infection.

• Pregnant women who have flu-like symptoms such as fever, cough, and sore throat should contact their pregnancy care provider immediately so that flu medications can be started and further instructions can be given. Women also may begin treating their fever with acetaminophen.

• Pregnant women also should speak to their pregnancy care provider if they have come in close contact with someone who has flu-like symptoms.

• All pregnant women should receive immunization for seasonal flu immediately and H1N1 flu as soon as the vaccine becomes available. The immunizations pregnant women receive are safe and provide flu protection for themselves and their newborns.

• Pregnant women can protect themselves from the flu by washing their hands frequently, by encouraging their family to do the same, and by avoiding contact with sick people.[3]

Your facility might be administering flu vaccinations. While the government is providing the H1N1 vaccine and administration supplies for free, providers cannot charge for the vaccine, but providers can charge for administering the injection. Use the following CPT codes issued by the American Medical Association that are specific to the H1N1 vaccine product: 90470 — H1N1 immunization administration (intramuscular, intranasal), including counseling when performed, and 90663 — Influenza virus vaccine, pandemic formulation, H1N1.[3]

CNE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the articles, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers and refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **The semester ends with this issue. You must complete the evaluation form included in this issue and return it in the provided reply envelope that is addressed "Education Department" to receive a certificate of completion.** When your evaluation is received, a certificate will be mailed to you. ■

CNE/CME Questions

After reading *Contraceptive Technology Update,* the participant will be able to:

- **identify** clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services.
- **describe** how those issues affect services and patient care.
- **integrate** practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts.

21. The levonorgestrel intrauterine system Mirena has an approved indication for:

A. treatment of heavy menstrual bleeding in women who use intrauterine contraception as their method of pregnancy prevention.
B. treatment of endometriosis in women who use intrauterine contraception as their method of pregnancy prevention.
C. treatment of anemia in women who use intrauterine contraception as their method of pregnancy prevention.
D. treatment of oligomenorrhea in women who use intrauterine contraception as their method of pregnancy prevention.

22. Research findings indicate that rates of serious infection in the mifepristone/misoprostol regimen decreased after protocol was changed:

A. from oral to vaginal administration of mifepristone.
B. from vaginal to buccal administration of misoprostol.
C. when dosage of both drugs was decreased.
D. when dosage of both drugs was increased.

23. What material is used in the Durex Avanti Bare and LifeStyles Skyn male condoms?

A. Vulcanized rubber
B. Polyurethane
C. Polyisoprene
D. Lambskin

24. The vaccine studied in the Thai RV144 trial used what type of vaccine strategy?

A. Peptide vaccine
B. Triple-vaccine
C. Pseudovirion vaccine
D. Prime-boost regimen of two vaccines

Answers: 21. A; 22. B; 23. C; 24. D.

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Contraceptive Technology Update *is endorsed by the National Association of Nurse Practitioners in Women's Health and the Association of Reproductive Health Professionals as a vital information source for health care professionals.*

S·T·D QUARTERLY™

HIV vaccine update: Progress made, but more work is left to do in research

Encouraging news comes from the HIV vaccine research front, where an investigational vaccine regimen tested in a Thailand clinical trial has been shown to be well tolerated and to have a modest effect in preventing HIV infection.[1-3]

The Thai Phase III HIV vaccine study, also known as RV144, was designed to test the safety and effectiveness of a prime-boost regimen of two vaccines: ALVAC-HIV vaccine, which is a modified canarypox vaccine developed by Lyon, France-based Sanofi Pasteur, and AIDSVAX B/E vaccine, which is a glycoprotein 120 vaccine initially developed by Vaxgen and now licensed to the San Francisco-based Global Solutions for Infectious Diseases. The two vaccines are based on the subtype B and E HIV strains that commonly circulate in Thailand.

The trial, which opened in October 2003, enrolled 16,402 men and women ages 18-30. Study participants received the ALVAC HIV vaccine or placebo at enrollment and again after one, three, and six months. The AIDSVAX B/E vaccine or placebo was given to participants at three and six months. Participants were tested for HIV infection every six months for three years and were counseled on how to avoid becoming infected with HIV during each clinic visit.

An analysis of the findings indicates 74 of 8,198 placebo recipients became infected with HIV compared with 51 of 8,197 participants who received the vaccine regimen. This level of effectiveness in preventing HIV infection was found to be statistically significant. However, the vaccine regimen had no effect on the amount of virus in the blood of volunteers who acquired HIV infection during the study, scientists report.

"The Thai study demonstrates why the HIV vaccine field must take a balanced approach to conducting both the basic research needed to discover and design new HIV vaccines and, when appropriate, testing candidate vaccines in people," says **Margaret Johnston**, PhD, director of the

EXECUTIVE SUMMARY

An investigational vaccine regimen tested in a Thailand clinical trial has been shown to be well-tolerated and to have a modest effect in preventing HIV infection. The study examined a prime-boost regimen of two vaccines: the ALVAC-HIV vaccine, which is a modified canarypox vaccine, and the AIDSVAX B/E vaccine, which is a glycoprotein 120 vaccine.

- Scientists with the Thai study had hypothesized that the vaccine would reduce HIV acquisition by 50%. While the study results were statistically significant, they did not reach that level.
- U.S. enrollment for a study of an exploratory HIV vaccine. The study will examine whether a two-part vaccine regimen can decrease viral load in study participants who later become infected with HIV.

Statement of Financial Disclosure:
Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, Associate Publisher **Coles McKagen**, and Senior Managing Editor **Joy Dickinson** report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. **Sharon Schnare** (Nurse Reviewer) discloses that she is a retained consultant and a speaker for Barr Laboratories, Berlex, and Organon; she is a consultant for 3M Pharmaceuticals; and she is a speaker for FEI Women's Health, Ortho-McNeil Pharmaceuticals, and Wyeth-Ayerst Pharmaceuticals.

Vaccine Research Program within the National Institute of Allergy and Infectious Diseases' (NIAID) Division of AIDS. "Both avenues provide critical information that will continue to help us better understand what is needed to develop a fully protective HIV vaccine."

Scientists say more information will come with the extended results of the follow-on study, RV152, due in 2013. The prospective cohort study will examine the virological, immunological, and clinical course of the HIV-infected vaccinees.[4]

Scientists with the RV144 study had hypothesized that the vaccine would reduce HIV acquisition by 50%. The study results were statistically significant, although they did not reach the level that had been specified, says **Larry Corey**, MD, co-director of the Vaccine and Infectious Disease Institute at Fred Hutchinson Cancer Research Center and the principal investigator of the HIV Vaccine Trials Network (HVTN), both based in Seattle.

"While these results are not at the level we will need to effectively control the AIDS pandemic, it is an indication that scientists will reach the goal of developing an effective HIV vaccine," says Corey. "There are several other vaccine candidates in the research pipeline and today's encouraging results will provide renewed enthusiasm for human clinical trials, as well as additional HIV vaccine discovery."

Advancing research into Phase III testing has been a daunting prospect for researchers. HVTN does not have any Phase III trials at this time, says **Sarah Alexander**, organization spokeswoman.Two trials, HVTN 502 (also known as the Step Study) and HVTN 503 (Phambili) were Phase 2B test of concept trials. Both were stopped in 2007 after an analysis of the Step Study indicated that the study would not be able to achieve positive results, she notes. ***(Contraceptive Technology Update* reported on the decision in the article, "Researchers halt HIV vaccine trial — What's the next step?" December 2007, p. 129.)**

HVTN is moving forward in vaccine development, as enrollment has begun in an exploratory HIV vaccine clinical study that will examine whether a two-part vaccine regimen can decrease viral load in study participants who later become infected with HIV. The study is enrolling men who have sex with men. Pending final site approvals, the study will be conducted in Atlanta; Bethesda, MD; Birmingham, AL; Boston; Chicago; Los Angeles; Nashville; New York City; Philadelphia; Rochester; San Francisco; and Seattle. *(Editor's note: For more information on enrollment, visit the study's web site, www.Hopetakesaction.org.)*

HVTN 505 is a Phase II, randomized, placebo-controlled, double-blind clinical trial. It employs a prime-boost strategy of two investigational vaccines developed by scientists at NIAID's Vaccine Research Center: a series of three immunizations with recombinant DNA-based vaccine over eight weeks, followed by one shot of a recombinant vaccine based on a weakened adenovirus Type 5 that carries the vaccine contents and helps stimulate the immune system. Of the 1,350 participants slated for enrollment, half will receive the investigational vaccine regimen, and half will receive placebo injections.

As an exploratory study, HVTN 505 is not part of a typical product development path of studies that leads to vaccine licensure; rather, it serves as the basis for subsequent research that will build upon its findings, explain HVTN officials.

Why test an HIV vaccine that is not intended or expected to prevent HIV infection? As the NIAID explains in a question and answer sheet: "A vaccine that reduces viral load in people infected with HIV would be a significant scientific breakthrough. Reducing viral load is important because typically people infected with HIV who have lower viral loads take longer to become sick and develop symptoms of AIDS. People with reduced levels of virus may also have a diminished ability to transmit the virus to others. Therefore, an HIV vaccine that reduces viral load may benefit a vaccinated individual who later becomes infected with HIV by delaying the onset of illness and the lifetime need for antiretroviral medicines. It may also benefit the public health by reducing HIV transmission to uninfected people."[5]

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Research eyes ring for microbicide delivery

Women in the United States now account for more than one-quarter of all new HIV/AIDS diagnoses.[1] To combat the epidemic, the National Institutes of Health has awarded Albert Einstein College of Medicine of Yeshiva University in Bronx, NY, a four-year, $7.2 million grant to develop a microbicide-releasing intravaginal ring to prevent HIV transmission.

"While condoms are excellent at preventing the transmission of HIV, it's often difficult for women to negotiate their use," says **Betsy Herold**, MD, professor of pediatrics, microbiology & immunology, and obstetrics & gynecology and women's health at Einstein, who will serve as principal investigator for the research. "It's imperative that women have alternative strategies available to protect their own health."

Much research effort is being aimed at developing coitally-independent, sustained release formulations for long-term administration of HIV microbicides. Vaginal ring devices are at the forefront of this formulation strategy.[2]

Intravaginal rings offer a variety of benefits for microbicide delivery, observes **Patrick Kiser**, PhD, associate professor of bioengineering at the University of Utah's College of Engineering, another principal investigator in the proposed research. They are particularly easy to use and can last for a long time, which makes patient compliance with the therapy much higher than with other dosage forms, Kiser notes.

Because rings can be placed in the vagina before sex, they offer protection to women who might not be able to negotiate condom use with their partners. Many men, particularly with the kind of rings being developed at the University of Utah, cannot detect the presence of the ring in the woman's vagina, says Kiser.

Kiser's research group is examining the use of thermoplastic elastomers to construct intravaginal rings. Such rings have been shown in vitro to be capable of sustained delivery of antiviral compounds over 30 days.[3] The Utah scientists are evaluating several intravaginal ring designs that are capable of delivering hydrophilic and hydrophobic drugs simultaneously in the vaginal lumen.

Focus on anti-HIV microbicides

Herold and colleagues will look at several anti-HIV microbicides, focusing on a two-drug combination for ring delivery. By targeting HIV infection at different steps very early in its life cycle, scientists hope to prevent the establishment of infection, she notes. Potential drug candidates include tenofovir, which is used as an oral systemic therapy against HIV, but which also has shown promise as a topical microbicide.[4] **(*Contraceptive Technology Update* reported on tenofovir research in "Tenofovir eyed as potential microbicide," May 2008, *STD Quarterly* supplement, p. 3.)** The team also will examine fusion inhibitors, such as maraviroc and PIE12-trimer, which block the virus from entering target immune cells by different mechanisms.

"We've deliberately chosen to focus on drugs that have already been approved for systemic use or are far along in the regulatory process," says Herold. "This should shorten the time it takes to begin clinical trials."

Safety is an important issue in development

EXECUTIVE SUMMARY

To combat the epidemic of HIV, the National Institutes of Health has awarded Albert Einstein College of Medicine of Yeshiva University a $7.2 million grant to develop a microbicide-releasing intravaginal ring to prevent HIV transmission.

- Researchers at the University of Utah are joining the investigation to examine the use of thermoplastic elastomers in developing intravaginal rings.
- Potential drug candidates include tenofovir, which is used as an oral systemic therapy against HIV but which also has shown promise as a topical microbicide. Fusion inhibitors, such as maraviroc and PIE12-trimer, which block the virus from entering target immune cells by different mechanisms, also will be considered.

and use of rings for microbicide delivery, says Herold. The configuration of cells in the vaginal epithelium form an impermeable barrier to HIV; if a microbicide disrupts the barrier, HIV may be able to slip through the gaps and infect circulating T cells, as evidenced by earlier work by Herold's research team.[5]

These findings are leading Herold's team to search for the right combinations to preserve the protective barrier in the vaginal epithelium, while adding drugs that will be at the right place, at the right time, when the virus presents. The ring, which can provide sustained delivery of a microbicide over three to four weeks, offers promise as a delivery candidate, Herold contends.

"There are hurdles to go, I think it's a really exciting area, and I think we will get there," she says. "I'm optimistic, but I think it is going to take some very careful, rigorous science to make sure that we address all the right questions before we start doing large-scale clinical trials."

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CTUPDATES

News ■ Resources ■ Events

Circle the dates for 2010 conferences

Update your clinical practice; make your plans now for the following 2010 conferences:

The 2010 National STD Conference at the Omni Hotel in Atlanta will address sexual health issues and review future directions for the field. The conference will include 30 abstract-driven oral sessions, symposia, and workshops. Online registration is available at the conference web site, www.cdc.gov/stdconference. Early-bird registration fee is $240, preregistration fee is $265, and late/on-site fee is $290. A limited number of $140 student registrations are available. Student identification is required.

Get up to speed on the latest in reproductive health at the 2010 sessions of the *Contraceptive Technology* conference. The first session is scheduled for March 25-27 in San Francisco, with a following session scheduled for April 15-17. Registration and program information are available at the Contemporary Forums web site, www.contemporaryforums.com. Click on the "Conference Calendar" and click on the conference title for pertinent information. ■

Give young teens info on building strong bones

If your practice includes treatment of young teens, check out new information provided by Best Bones Forever!, a national bone health campaign aimed at helping girls ages 9-14 and their parents understand the importance of building strong bones for life.

The campaign, developed by the U.S. Department of Health and Human Services' Office on Women's Health, encourages girls and their BFFs (best friends forever) to eat more foods with calcium and vitamin D and get lots of physical activity, particularly activities that involve running and jumping.

Best Bones Forever! has a web site just for girls at www.bestbonesforever.gov, as well as information for parents at a companion site, www.bestbonesforever.gov/parents. The girls' site has several interactive elements, such as a calcium calculator to check calcium intake from different foods, plus easy-to-understand information on bone health issues. ■

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2009 Index

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